2.0 NON-TECHNICAL ABSTRACT

Lower extremity peripheral arterial disease (PAD) is increasingly prevalent in the United States. It is currently estimated to affect 8 to 12 million individuals. One-third to one-half of these patients suffer from a severe form known as intermittent claudication (IC). Individuals with PAD and IC have a reduced functional capacity, lower quality of life, and an extremely high risk of cardiovascular morbidity and mortality. Management of risk factors, lifestyle interventions, and pharmacologic treatment with agents to provide symptomatic relief have a central role in improving function, quality of life and retarding the progression to advanced endpoints such as rest pain, non-healing ulcers, gangrene and cardiac death. Surgical or percutaneous revascularization for aorto-iliac disease provides durable treatment for individuals with disabling symptoms. Infra-inguinal disease, even if extensive, very rarely justifies surgical intervention for claudication. The current therapeutic options available to patients with symptomatic IC are primarily exercise, pentoxifylline, and cilostazol. However, the effectiveness of these drugs is limited.

VLTS-589 is a non-viral, plasmid-DNA investigational drug that contains the gene encoding for the human developmentally-regulated endothelial locus (Del-1). In animal models, it has been shown to elicit new vessel formation. For the evaluation in subjects with intermittent claudication, VLTS-589 is administered by intramuscular injection (IM) into the diseased limb. In previous animal safety studies, VLTS-589 has not elicited any adverse effects. An ongoing Phase I safety trial in humans also has not shown any adverse effects.

The proposed Phase II trial is a multi-center, double-blind, placebo-controlled trial designed to evaluate the safety and tolerability of VLTS-589 in subjects with intermittent claudication secondary to peripheral arterial disease and to evaluate the effect on the subject's peak walking time (treadmill) at the end of day 90 compared to placebo. Following the completion of the currently ongoing Phase I safety trial, the proposed Phase II trial will enroll approximately 100 subjects; half of which will receive a placebo in place of the investigational drug.